



**Naval Hospital
Jacksonville**

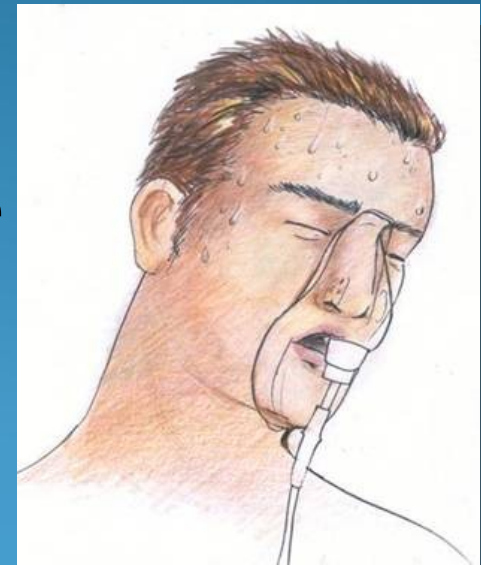
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Pulmonary and Critical Care Medicine

Management of Severe H1N1 Influenza Respiratory Infection

OUTLINE

- Clinical features and risk factors for severe pandemic H1N1 influenza respiratory infection
- Antiviral and other drug therapy
- Ventilatory and non-ventilatory strategies for managing patients with life threatening H1N1 related influenza respiratory failure

- ❑ 47 yo male. Chief Complaint: SOB, aches, fever, chills x 12 hours
- ❑ Past medical history:
 - ❑ Severe asthma, prior ICU admission
 - ❑ Heavy smoking
- ❑ ER screening:
 - ❑ Temperature 36.5, respiratory rate 38, BP 110/80, HR 98, saturation 91% on room air
 - ❑ Severe respiratory distress, unable to complete full sentences, agitated
 - ❑ Minimal wheezing on examination

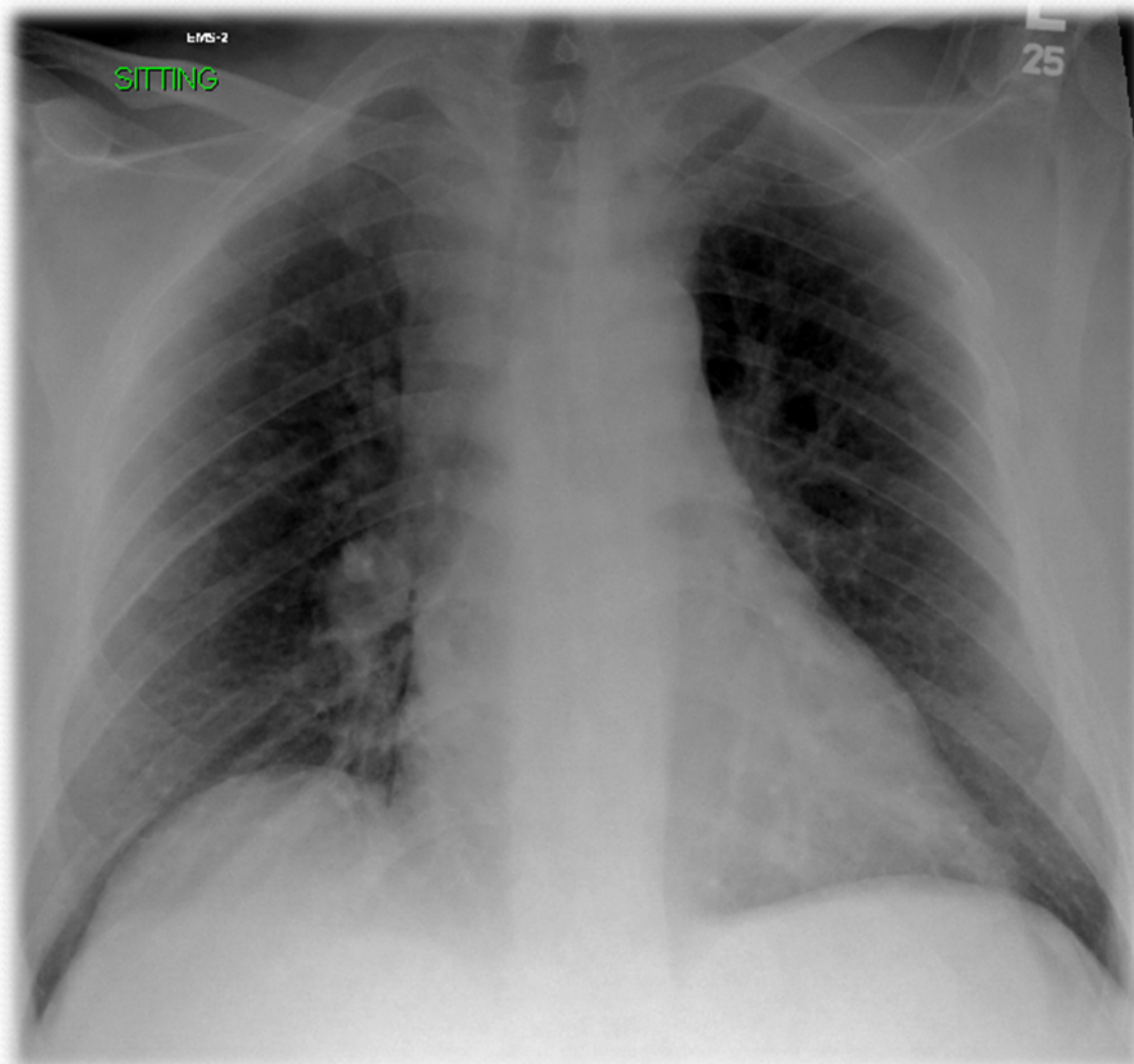


Laboratory tests

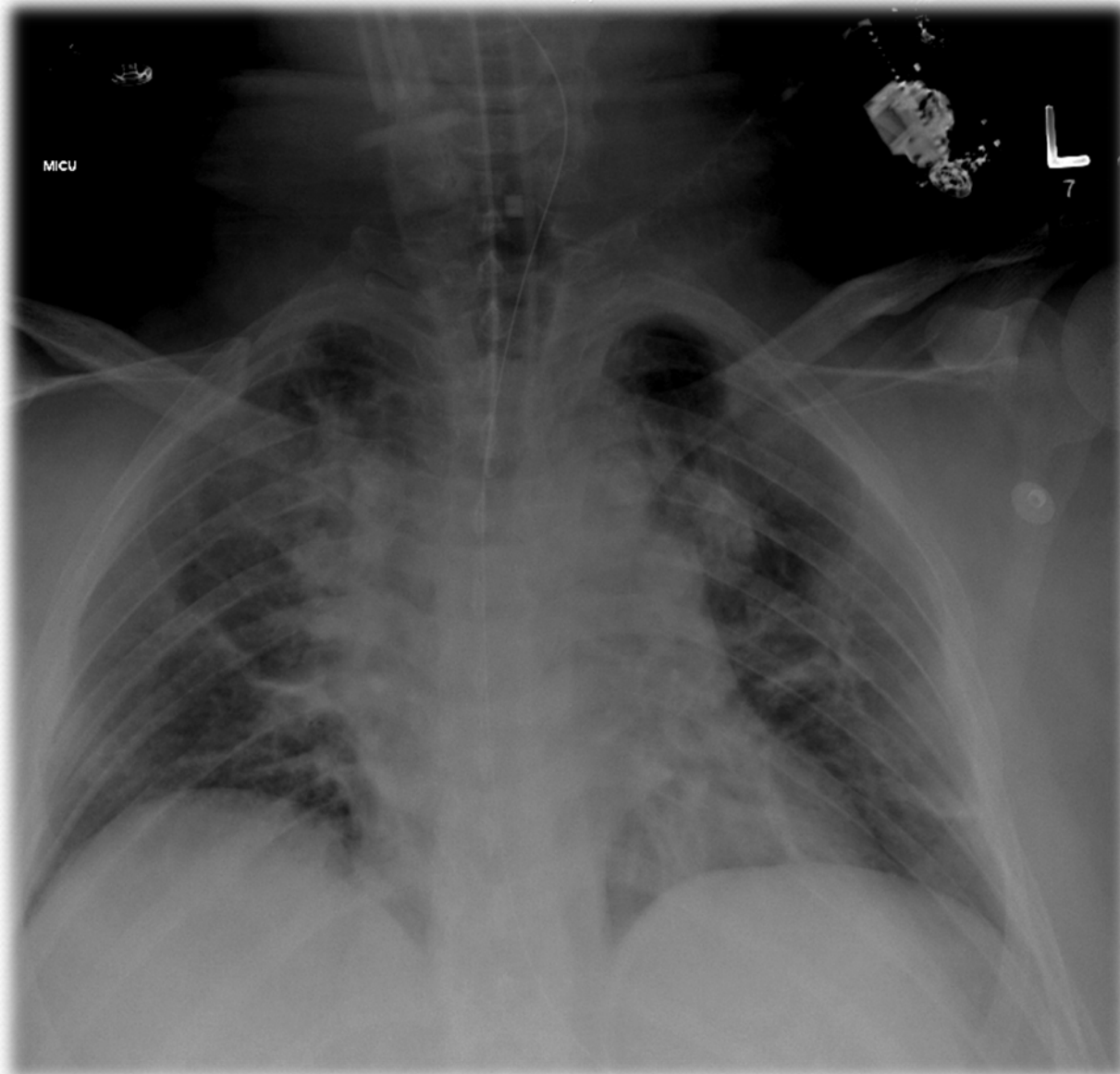
- WBC 12.6 (81% PMN, 5% lymphocytes)
- Hg: 14.6, Platelets: 300
- Urea 106, creatinine 1.2
- Bilirubin 2
- LDH 250, CK 670
- ABG: pH 7.23 PCO₂ 54, PO₂ 125, FiO₂ was 75%, PaO₂/FiO₂ ratio = 167
- Lactic acid 3.3
- Swine Flu PCR positive



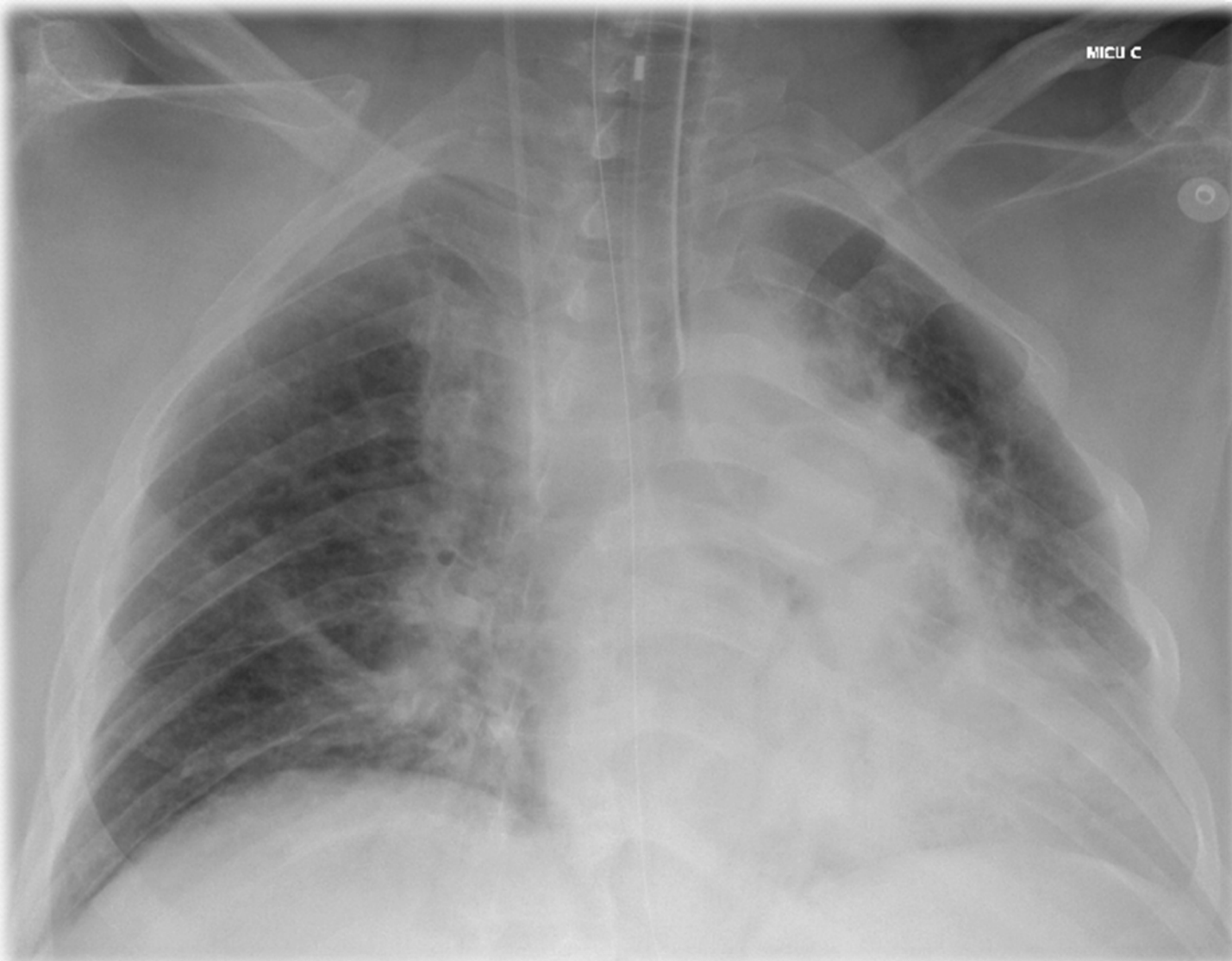
9/8/2009 PM



9/9/2009 AM



9/9/2009 PM



Severe H1N1 Influenza Respiratory Infection

- **Common feature is severe hypoxemia, ARDS refractory to conventional ventilation**
- **Respiratory presentations**
 - **Viral pneumonitis**
 - **Exacerbations of chronic lung, cardiac disease**
 - **Secondary bacterial pneumonia**
 - **Croup/bronchiolitis in children**
- **High case fatality rates due to multiple organ failure have been**

Risk Factors for Severe Disease

- **Underlying medical conditions**
 - **Asthma, COPD**
- **Obesity**
- **Pregnancy**
- **Young children**

Severe 2009 H1N1 Respiratory Infection

- **US study:**
 - **67 (25%) of 272 hospitalized patients needed ICU**
 - **28% mortality (16% deaths were pregnant pts)**
- **Spain study:**
 - **First 32 patients admitted to the ICU**
 - **25% mortality**
- **Australia and New Zealand study:**
 - **722 critically ill patients (9% pregnant)**
 - **14% mortality**

Fatal H1N1 Influenza Respiratory Infection

- **Autopsy findings of 21 Brazilian patients**
- **72% between age 30-59**
- **The cause of death in all patients was extensive lung involvement**
- **No direct signs of virus-induced disease in the other examined organs**

Mauad, T. A J Respir Crit Care Med
2010

Deaths in Pregnant Women due to Pandemic (H1N1) 2009 Influenza

United States, April 15 to June 16, 2009

<i>Case #</i>	<i>Age (years)</i>	<i>Weeks' gestation</i>	<i>Underlying Medical Conditions</i>
1	33	35	Mild asthma, psoriasis
2	24	32	Obesity
3	20	27	None
4	21	11	Factor V Leiden deficiency
5	22	36	None
6	30	30	None

Jamieson DJ et al., Lancet 374:451-8, 2009

Deaths among Pregnant Women

- **All developed primary viral pneumonia with subsequent ARDS requiring mechanical ventilation**
- **Pregnancy outcomes: 5 with cesarean delivery (27-36 weeks gestation) - 3 in ICU or ED, 1 fetal loss at 11 weeks**
- **Time from symptom onset to receipt of antiviral medication was 6-15 days (median 9)**
- **Time from presentation for medical care until receipt of antiviral treatment was 2-14 days (median 4.5)**

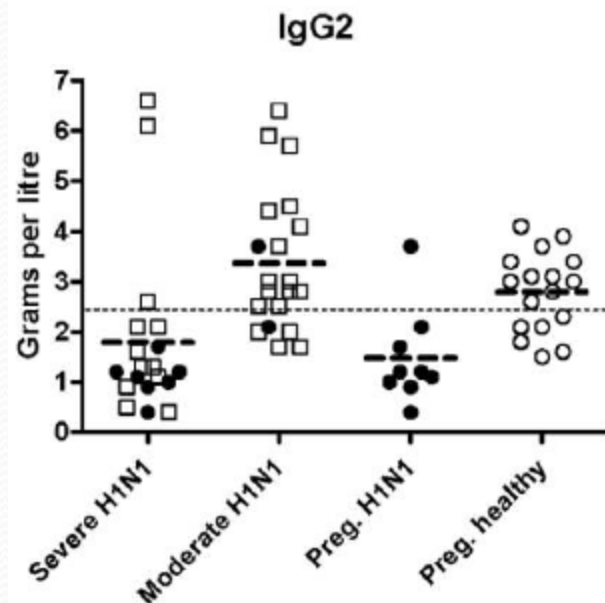
Why are pregnant women at increased risk for severe influenza illness?

- Mechanical, hormonal, immunologic alterations in pregnancy
- Changes in respiratory and cardiovascular systems - increased heart rate, stroke volume, and oxygen consumption; decreased lung volumes
- Immunologic changes - shift away from cell-mediated immunity
- These changes render pregnant women more susceptible and more severely affected by certain viral pathogens

Association between Severe Pandemic 2009 Influenza A (H1N1) Virus Infection and Immunoglobulin G₂ Subclass Deficiency

C. L. Gordon,¹ P. D. R. Johnson,^{1,10} M. Permezel,⁵ N. E. Holmes,¹ G. Gutteridge,² C. F. McDonald,³ D. P. Eisen,^{6,10} A. J. Stewardson,⁶ J. Edington,⁷ P. G. P. Charles,¹ N. Crinis,⁴ M. J. Black,⁸ J. Torresi,^{1,10} and M. L. Grayson,^{1,4,9,10}

¹Infectious Diseases, ²Intensive Care, ³Respiratory, and ⁴Pathology Departments, Austin Health, ⁵Department of Obstetrics and Gynaecology, Mercy Hospital for Women, ⁶Victorian Infectious Diseases Service, Royal Melbourne Hospital, University of Melbourne, Melbourne, ⁷Intensive Care Unit, Bendigo Health, ⁸Pathology Department, Alfred Health, ⁹Department of Epidemiology and Preventive Medicine, Monash University, and ¹⁰Department of Medicine, University of Melbourne, Melbourne, Australia



Ventilator Management



ARDS Net Low-Stretch Ventilation Study

- **Test of low vs. “standard” lung volume stretch**
 - 6 vs 12 mL/kg (Ideal Body Wt)
 - PEEP and FIO₂ controlled by protocol
- **Decreased mortality**
 - 40% to 31%
- **VILI/Biotrauma contributes to mortality**

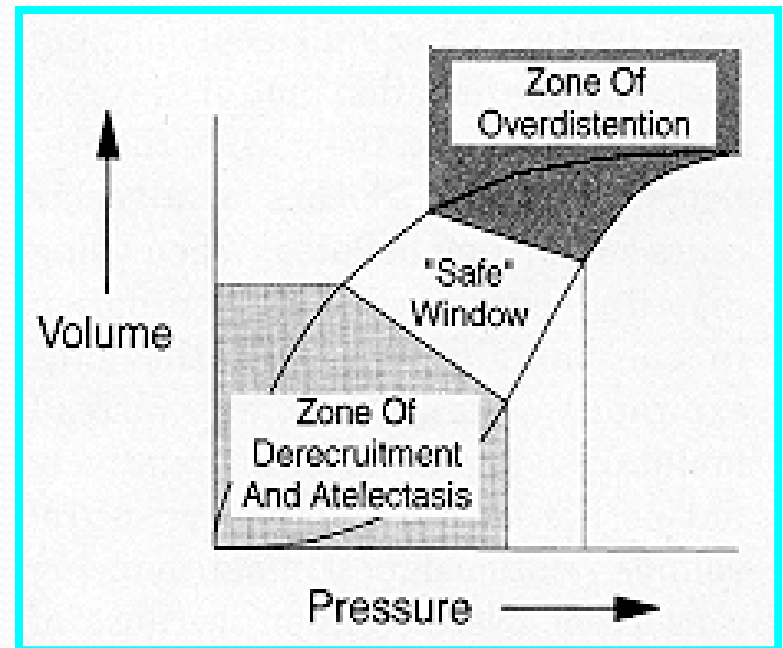


ARDSNET

NEJM 2000

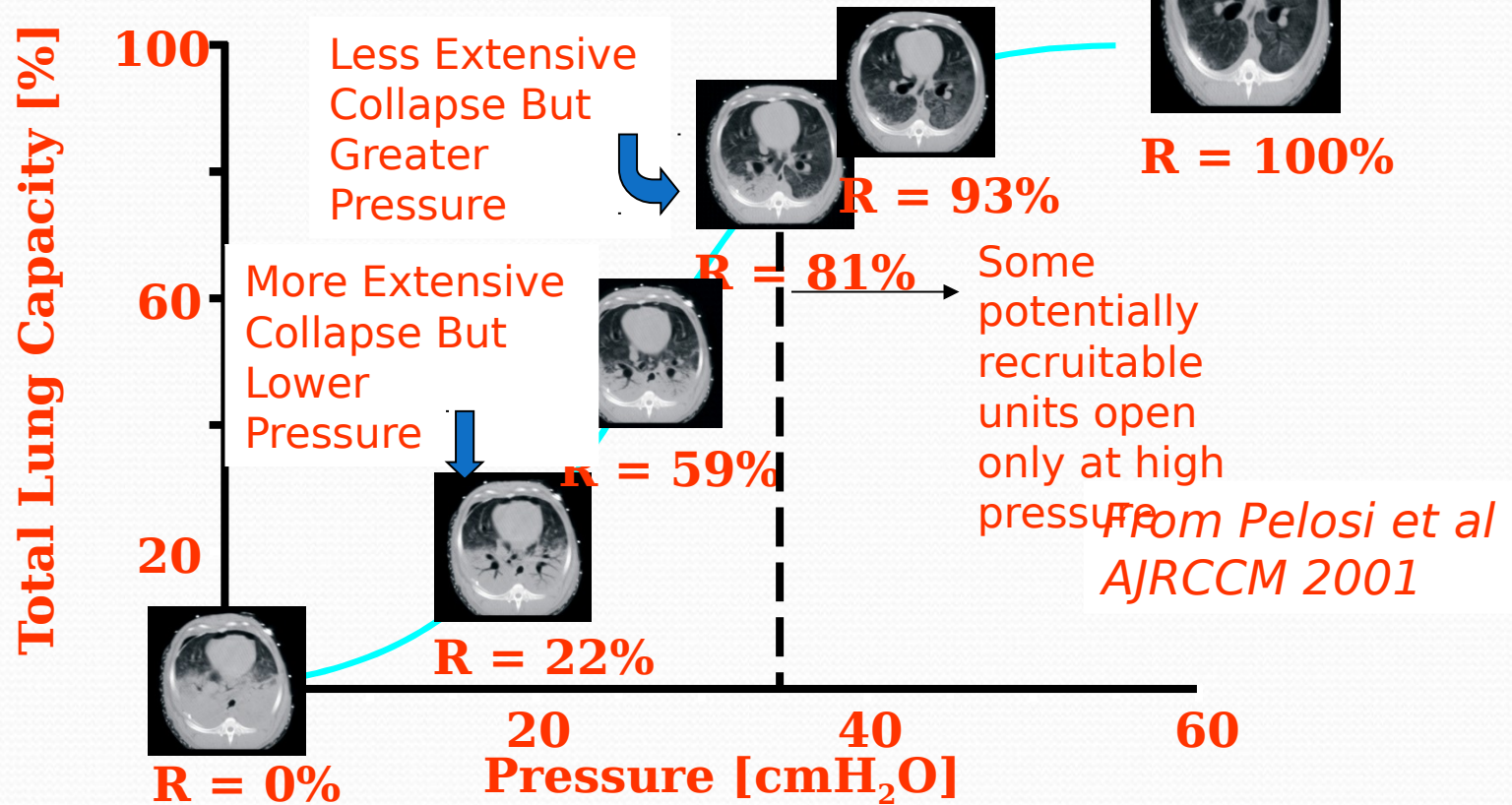
Pulmonary Injury Sequence

- There are two injury zones during mechanical ventilation
 - Low lung volume ventilation tears adhesive surfaces
 - High lung volume ventilation overdistends, resulting in “Volutrauma”
- The difficulty is finding the “Safe Window”

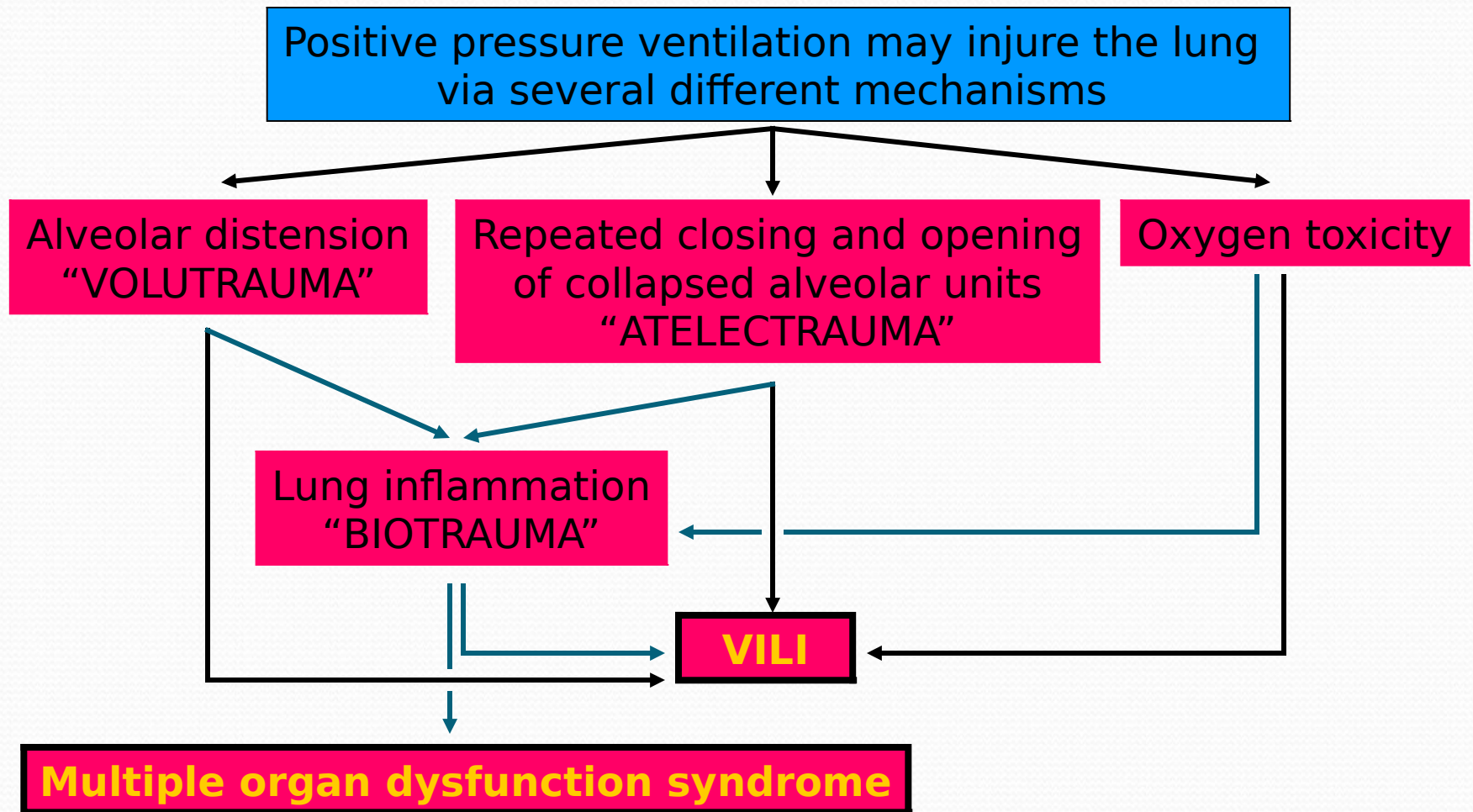


Froese AB, Crit Care Med 1997; 25:906

How Much Collapse Is Dangerous Depends on the Alveolar (Plateau) Pressure



Search for ventilatory “lung protective” strategies



Mechanical Ventilation for ARDS in Pregnant Patients

- May have to accept higher alveolar pressures than 30-35 cm H₂O due to reduced thoracic compliance
- Arterial oxygenation goals $\geq$ or equal to 92% for fetal protection
- Mild to moderate permissive hypercapnea probably acceptable
- X ray radiation
- Sedatives crossing the placenta



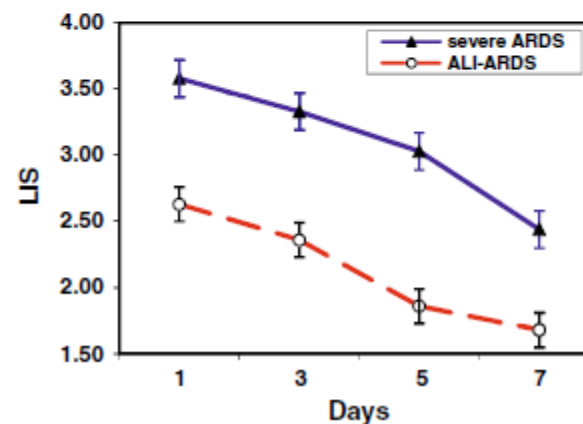
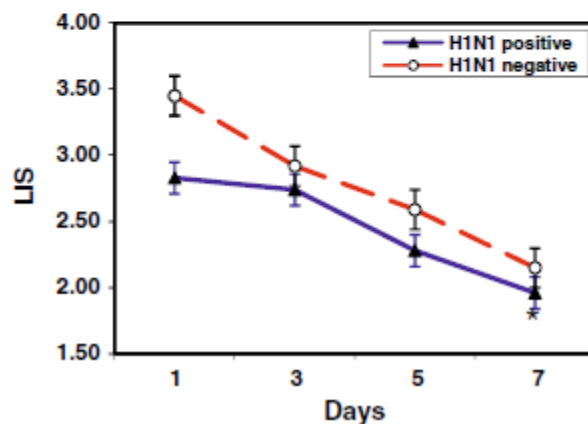
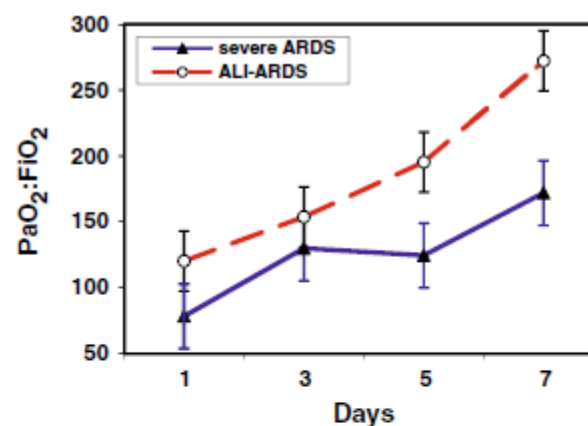
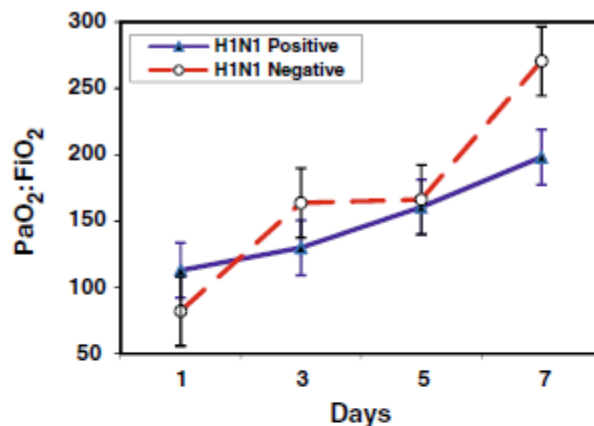
Other Therapy

ARDS: Treatment

- Glucocorticoids
 - No proven benefits in acute phase
 - Some evidence of improvement during proliferative phase (*Meduri et al JAMA 1998;280:159-165*)
 - Methylprednisolone 2 mg/kg initially for 32 days
 - Improvement in Lung injury scores, MOSD scores and mortality
 - Benefits may be noticed by day 3
 - Concern for high risk of infection

Adolfo Maximo Quispe-Laime
Jonas Daniel Bracco
Patricia Alejandra Barberio
Claudio German Campagne
Verónica Edith Rolfo
Reba Umberger
Gianfranco Umberto Meduri

H1N1 influenza A virus-associated acute lung injury: response to combination oseltamivir and prolonged corticosteroid treatment



Antiviral Agents for H1N1 Influenza Infection

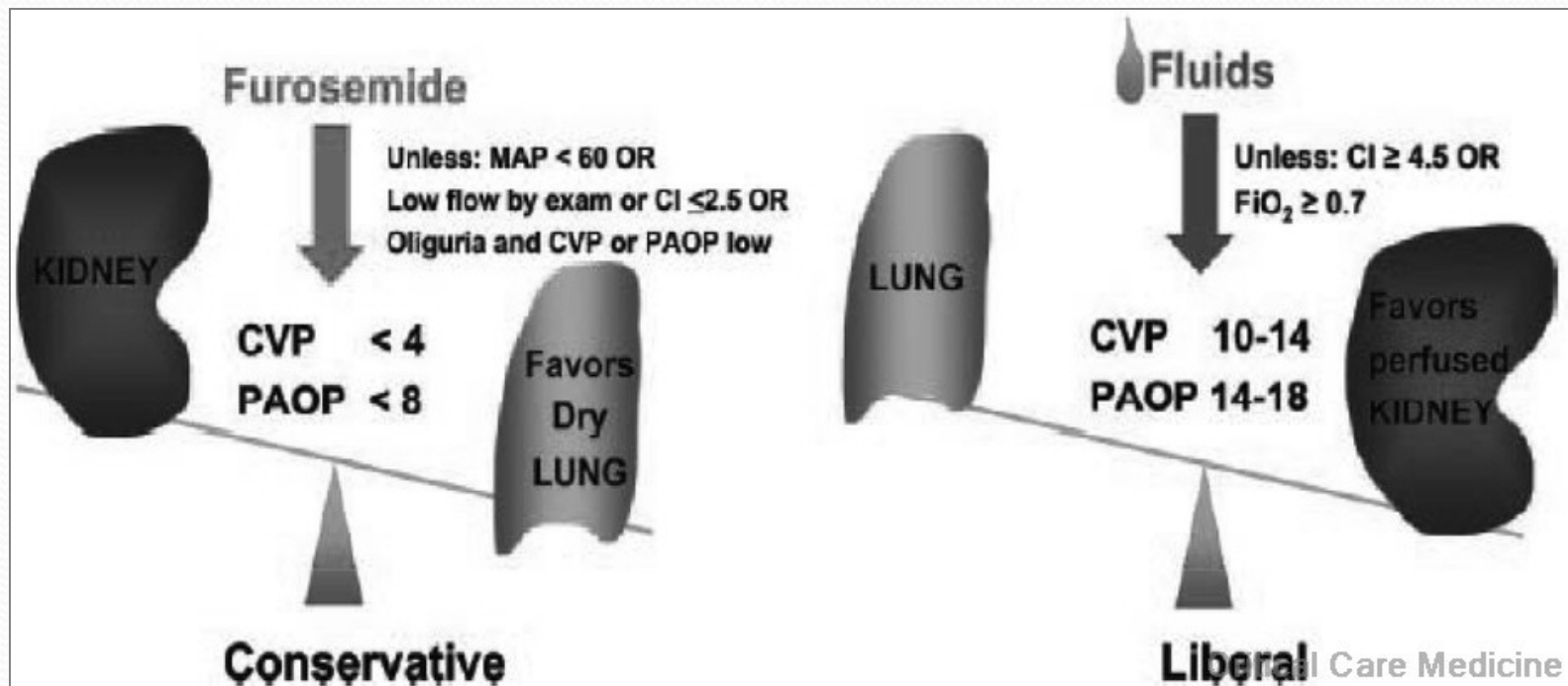
- **Oral Oseltamivir and inhaled Zanamivir**
 - **High dose Oseltamivir for severe cases**
- **28 reported isolates of resistant Oseltamivir**
 - **12/28 in patients who were prophylactically treated due to close contact**
 - **? IV Zanamivir**
- **Close monitoring of severely ill patients who do not respond to**

Antiviral Agents for H1N1 Influenza Infection

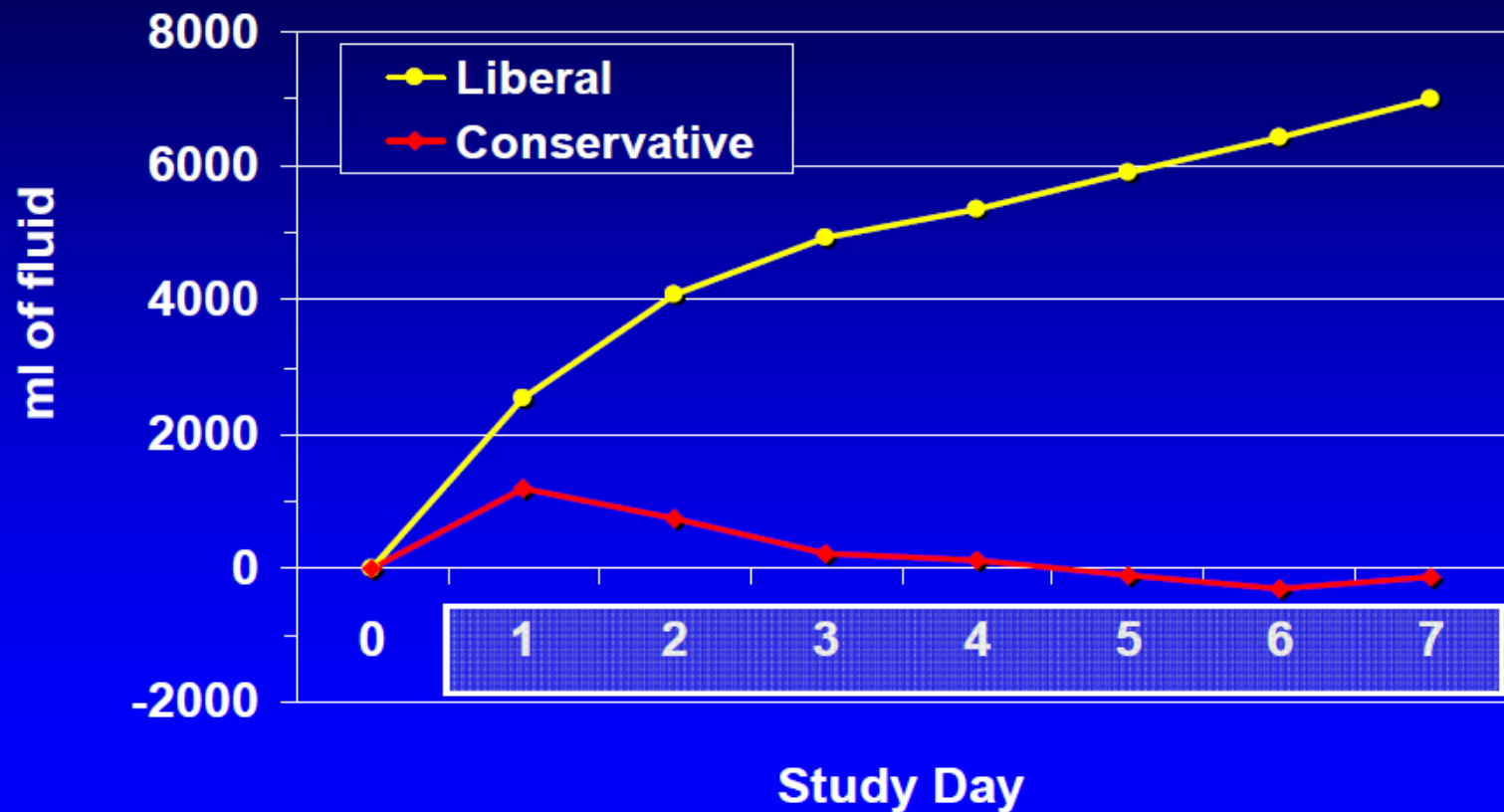
- **Chile: 2009 containment strategy in a large private facility**
 - **10,048 Emergency Dept visits with suspected H1N1 infection**
 - **Virtually all treated with neuraminidase inhibitor**
 - **2% cases hospitalized**
 - **11 patients admitted to the ICU without any deaths**

Torres JP, CID 2010

Fluid Management in Acute Lung Injury



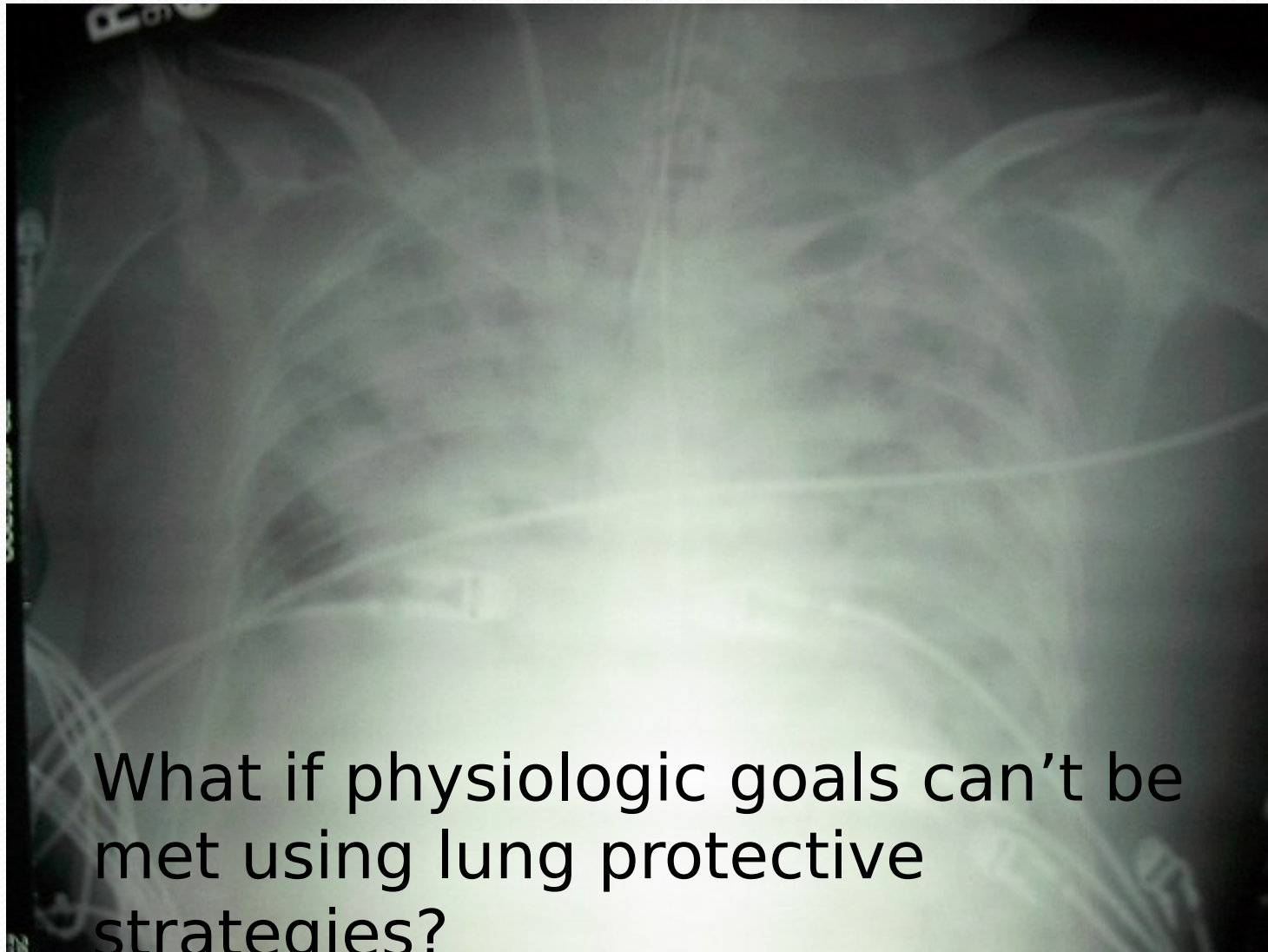
Cumulative fluid balance in FACTT



Fluid Management in Acute Lung Injury

- FACTT demonstrates that a fluid conservative approach reduces time spent on ventilator
- No conflict with early goal-directed therapy for sepsis

Wiedemann HP, N Engl J Med 2006



What if physiologic goals can't be met using lung protective strategies?



Rescue Therapies: Don't wait until too late

“Rescue” Therapies

- **Not proven to reduce mortality or improve other desirable outcomes (? ECMO)**
- **Physiologic benefit or improvement**
- **“Rescue” therapies include:**
 - **Alternates modes of ventilation:**
 - **High frequency oscillatory ventilation (HFOV)**
 - **Airway pressure release ventilation (APRV)**
 - **Prone positioning**
 - **Inhaled nitric oxide (iNO)**
 - **Extracorporeal life support (ECMO)**

High Frequency Oscillatory Ventilation (HFOV)

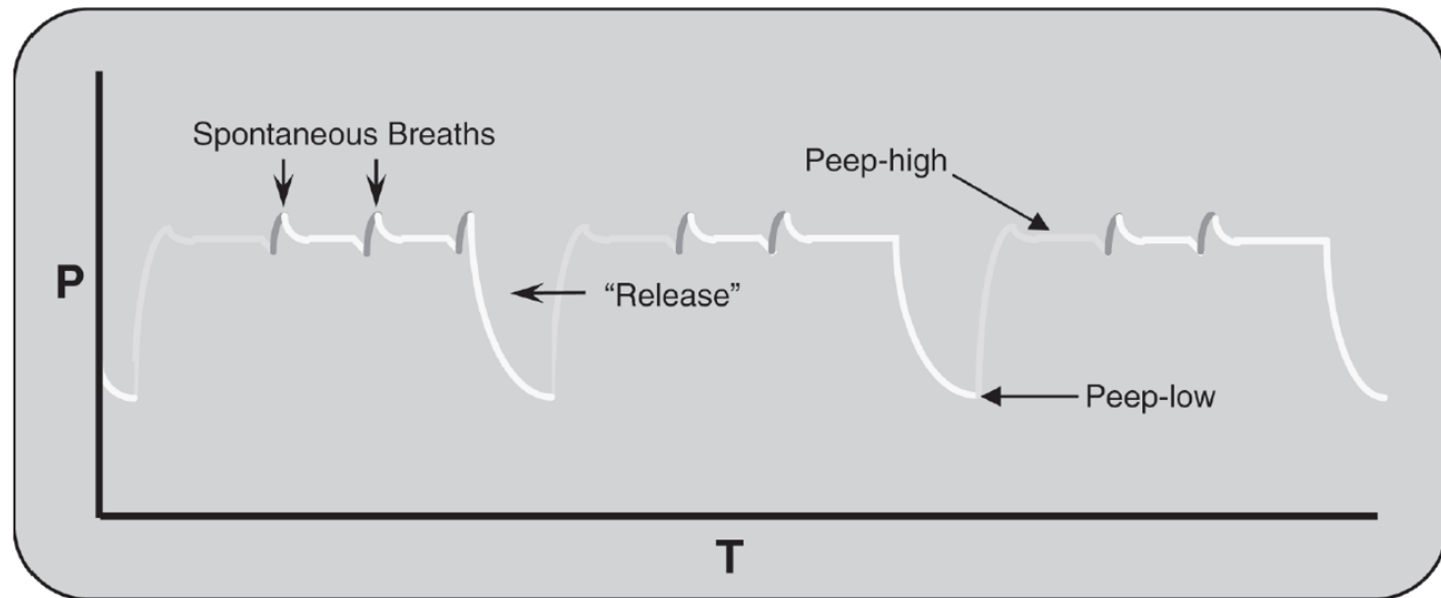
- When to consider HFOV use?
- As with all candidates, the earlier the better
 - $\text{FiO}_2 \geq 60$ despite max standard ventilation settings
- Relative contra-indications
 - Obstructive lung disease
 - Elevated intracranial Pressure



Airway Pressure Release Ventilation (APRV)



Figure 1. TYPICAL PRESSURE WAVEFORM OF APRV



Prone Positioning

- ✦ Limits the expansion of cephalic and parasternal lung regions
- ✦ Relieves the cardiac and abdominal compression exerted on the lower lobes
- ✦ Leads to more uniform regional ventilation/perfusion
- ✦ Facilitates drainage of secretions
- ✦ Potentiates the beneficial effect of recruitment maneuvers

Prone Positioning



Prone Positioning



Part 2 pumarejo h1n1.pptx

Prone Positioning

✦ **Absolute contraindications**

- Life-threatening circulatory shock
- Increased intracranial pressure

✦ **Main complications**

- Facial and periorbital edema
- Pressure sores
- Accidental loss-displacement medical devices
- Airway obstruction
- Hypotension
- Arrhythmias
- Vomiting

Inhaled Nitric Oxide (iNO)

- Can be delivered through ventilator circuit
- Increases blood flow in ventilated areas
- Improves ventilation-perfusion matching
- Low dose iNO improves short term oxygenation without improving duration of ventilation or mortality
- No significant complications associated with therapy

ECMO: Extra Corporeal Membrane Oxygenation



Circuit Pressure Monitors

Artificial Lung

Pump

Anticoagulation Level Test Device

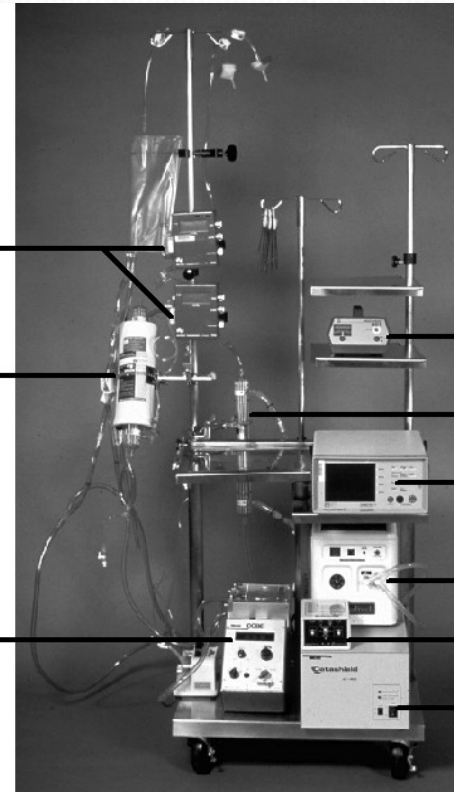
Heat exchanger

S_vO₂ Monitor

Heater Water Bath

Bladder box controller

Backup Battery



UK CESAR Trial

- **Conventional ventilation vs Conventional protocols with the option for ECMO**
- **Randomized 90 patients to each arm**
 - **Protocol including ECMO: 63% healthy survival**
 - **Control : 47% healthy survival**
- **Protocolized care including ECMO in an expert ARDS center yielded higher survival than the best standard care in tertiary ICUs in the UK**

Adult ECMO in Hypoxic Respiratory Failure Indications

- Potentially reversible respiratory failure refractory to maximal conventional treatment (50-80 % mortality risk)
- Ventilated < 7 days
- No contraindication to anticoagulation

ECMO Relative Contraindications

- Mechanical ventilation at high settings for 7 days or more
- Recent CNS hemorrhage or expanding
- Pharmacologic immunosuppression (Actual Neutrophilic Count < 400)

ECMO Complications

- Intracerebral hemorrhage
- Vascular complications
- Pulmonary hemorrhage (alveolar)
- Venous thromboembolism

ECMO for H1N1 Infection

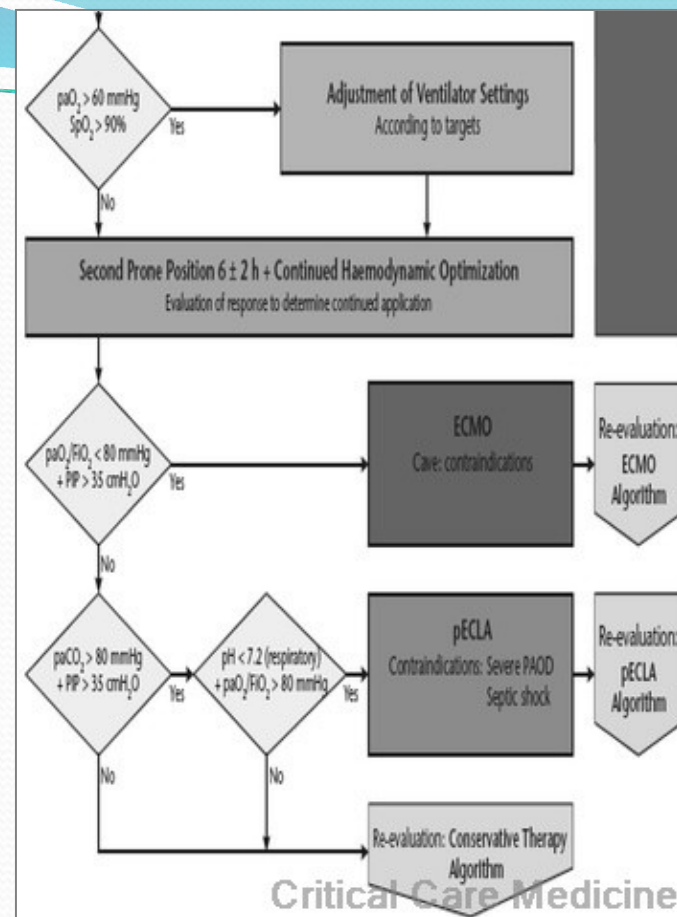
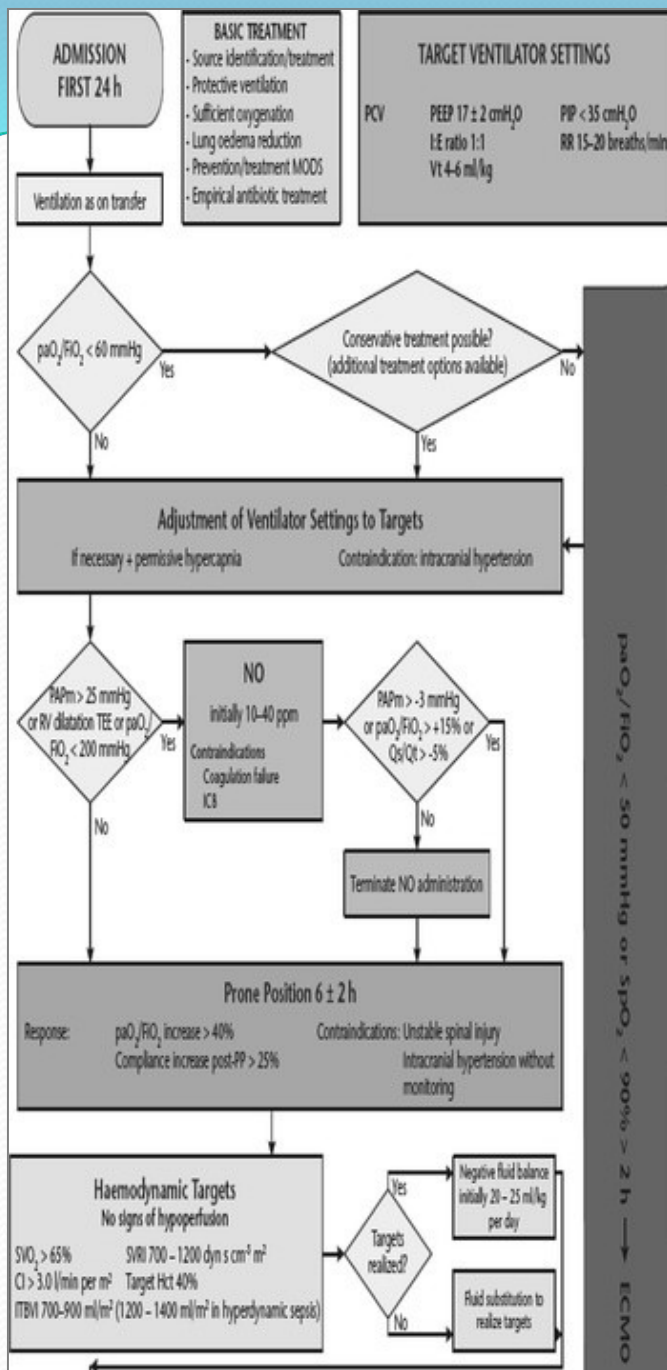
- **Australia and New Zealand ECMO influenza investigators**
- **201 ICU patients,**
 - **68 patients received ECMO**
 - **Age 34.4**
 - **Mean time on ECMO: 10 days**
- **70 % survival to hospital discharge**

Frittenbery et al JAMA 2009

H1N1 in ICU (Canada)

- **Rescue therapies**
 - **Paralysis: 28%**
 - **Nitric Oxide: 13.7%**
 - **High Frequency Oscillatory Ventilation: 11%**
 - **ECMO: 4.3%**
 - **Prone Positioning: 3%**
- **Overall ICU Mortality at 90 days: 17.3%**

Kumar A et al JAMA
2009;302



Severe H1N1 Influenza Respiratory Failure Management Protocol

Regional Centers for Delivery of ECMO



Steps for Surge Strategies

- **Develop regional triage plan**
- **Develop regional triggers**
- **Just in time education to reduce patient transfer**
 - **Telemedicine**
 - **Ventilator management standard**
- **Ventilators and supplies**

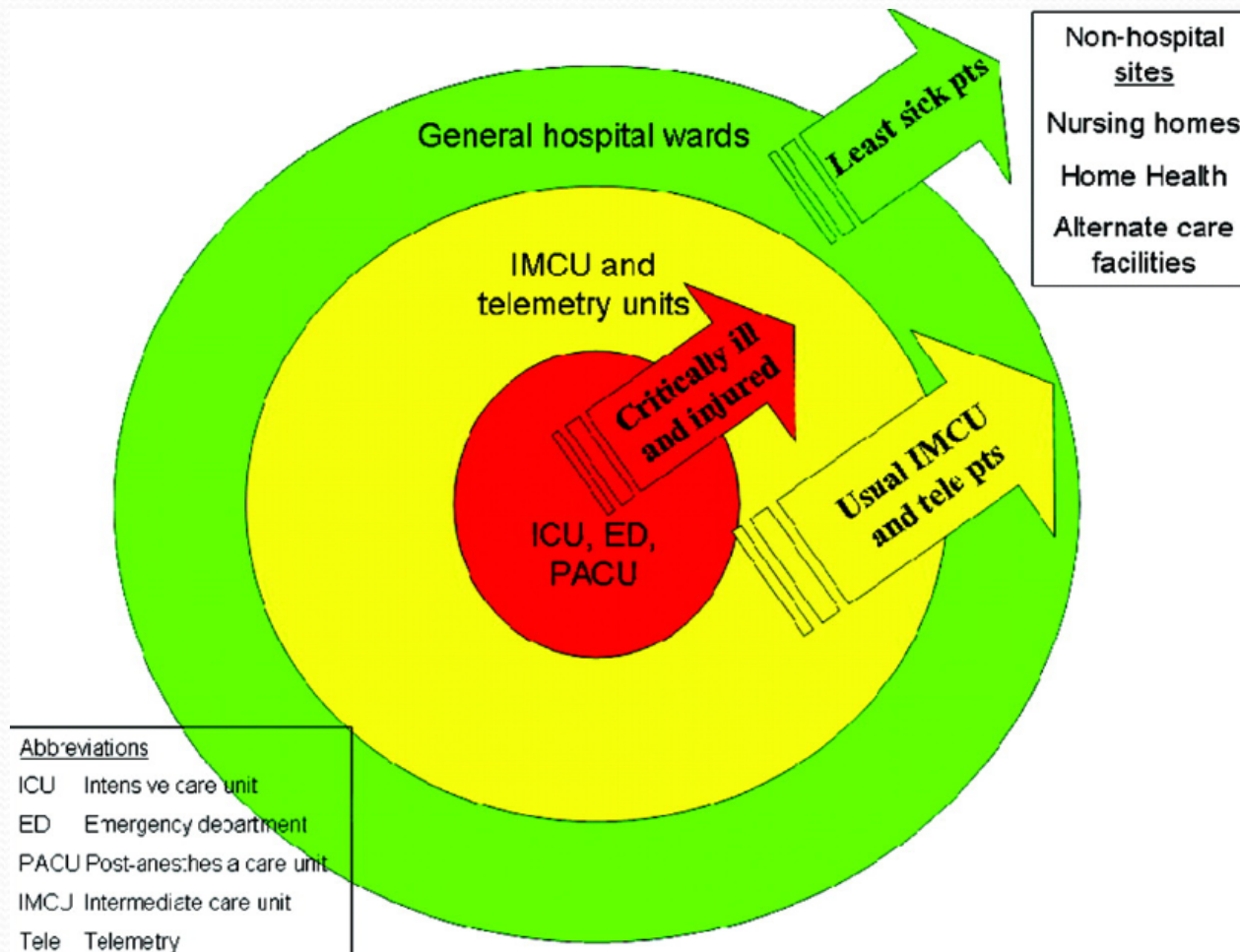
Surge Ventilators



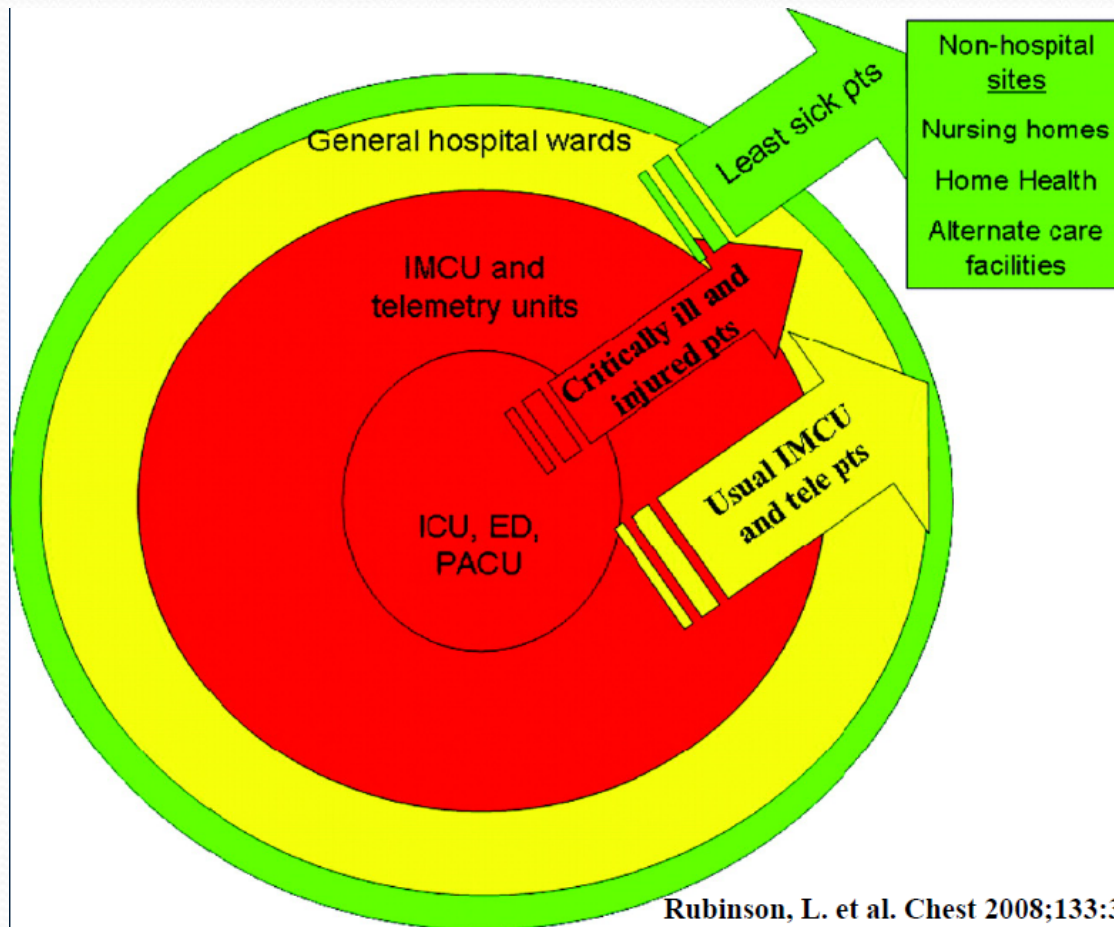
Sophisticated Transport Ventilators



Clinical space utilization



Clinical space utilization



Questions?

2009 H1N1

